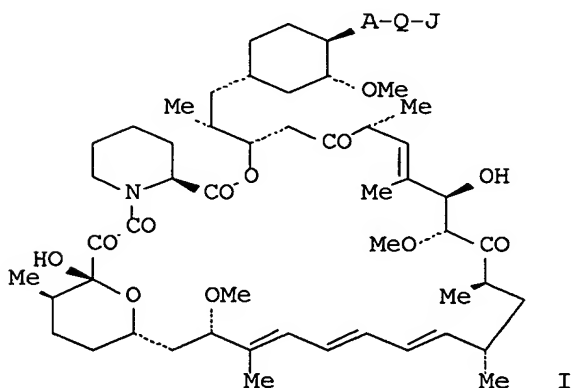


L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2004:310872 CAPLUS Full-text  
 DN 140:321159  
 TI Preparation of phosphorus-containing rapamycin derivatives for use in pharmaceutical compositions as immunosuppressive agents  
 IN Metcalf, Chester A.; Rozamus, Leonard W.; Wang, Yihan; Bernstein, David L.  
 PA USA  
 SO U.S. Pat. Appl. Publ., 55 pp., Cont.-in-part of U.S. Pat. Appl. 2003 220,297.  
 CODEN: USXXCO  
 DT Patent  
 LA English  
 FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004073024	A1	20040415	US 2003-635054	20030806
	US 2003220297	A1	20031127	US 2003-357152	20030203
	US 2005032825	A1	20050210	US 2004-862149	20040604
PRAI	US 2002-353252P	P	20020201		
	US 2002-426928P	P	20021115		
	US 2002-428383P	P	20021122		
	US 2002-433930P	P	20021217		
	US 2003-357152	A2	20030203		
	US 2003-635054	A2	20030806		
OS	MARPAT 140:321159				
GI					



AB Rapamycin derivs. containing a phosphorus moiety, such as I [A = O, S, NR<sub>2</sub>; Q = bond, aliphatic, heteroaliph., aryl, or heteroaryl moiety; J = P(O)(R<sub>5</sub>)<sub>2</sub>, P(O)(R<sub>5</sub>)(OR<sub>5</sub>), P(O)(R<sub>5</sub>)(NR<sub>2</sub>R<sub>5</sub>), P(O)(NR<sub>2</sub>R<sub>5</sub>)<sub>2</sub>, P(O)(OR<sub>5</sub>)(NR<sub>2</sub>R<sub>5</sub>); R<sub>2</sub>, R<sub>5</sub> = H, aliphatic, heteroaliph., heteroaryl, etc.], were prepared for therapeutic use as immunosuppressive agents. These rapamycin derivs. are useful for treatment of graft vs. host disease, lupus, rheumatoid arthritis, diabetes mellitus, myasthenia gravis, multiple sclerosis, psoriasis, dermatitis, eczema, seborrhea, inflammatory bowel disease, pulmonary inflammation, ocular uveitis; adult T-cell leukemia, lymphoma, fungal infections, hyperproliferative restenosis, graft vascular atherosclerosis, coronary artery disease, cerebrovascular disease, arteriosclerosis, atherosclerosis, nonatheromatous arteriosclerosis, or vascular wall damage from cellular events leading toward immune mediated vascular damage, stroke or multi-infarct dementia. Thus, I [A-Q-J = OP(O)(OEt)(Me)] was prepared by

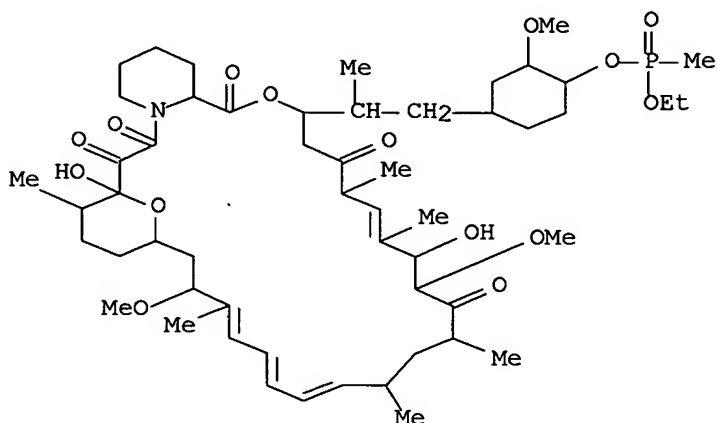
reacting rapamycin with Et methylphosphonochloridate using 3,5-lutidine in CH<sub>2</sub>Cl<sub>2</sub> under a nitrogen atmosphere. Binding affinity of the rapamycin phosphorus derivs. for human FKBP-12 protein was assayed, dosages for restenosis prevention were discussed.

IT 572924-46-0P 572924-47-1P 572924-48-2P  
572924-49-3P 572924-50-6P 572924-51-7P  
572924-52-8P 572924-53-9P 572924-54-0P  
572924-55-1P 572924-56-2P 572924-57-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of phosphorus-containing rapamycin derivs. for use in pharmaceutical compns. as immunosuppressive agents)

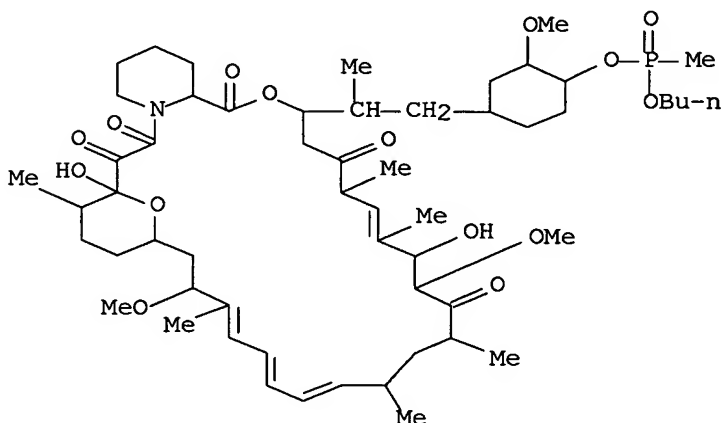
RN 572924-46-0 CAPLUS

CN Rapamycin, 42-(ethyl methylphosphonate) (9CI) (CA INDEX NAME)



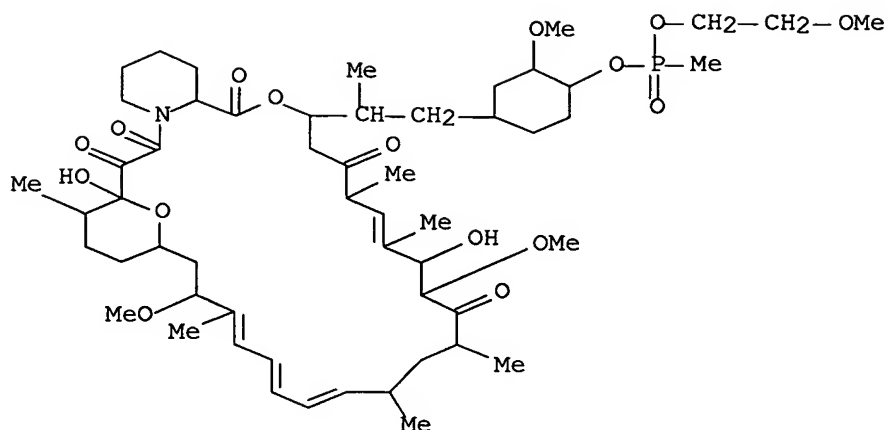
RN 572924-47-1 CAPLUS

CN Rapamycin, 42-(butyl methylphosphonate) (9CI) (CA INDEX NAME)



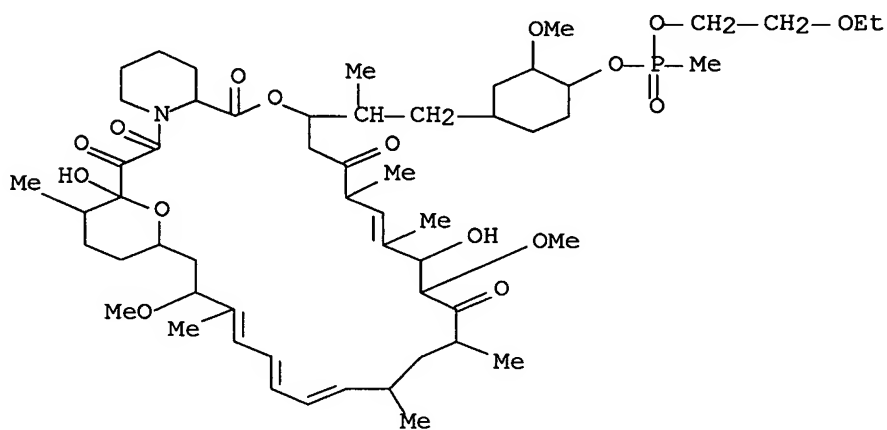
RN 572924-48-2 CAPLUS

CN Rapamycin, 42-(2-methoxyethyl methylphosphonate) (9CI) (CA INDEX NAME)



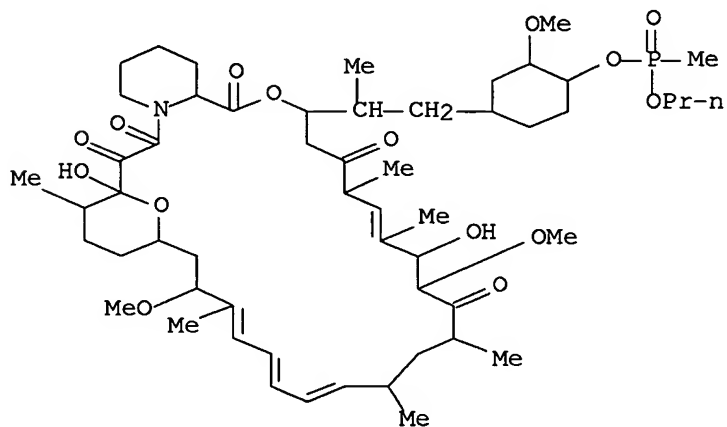
RN 572924-49-3 CAPLUS

CN Rapamycin, 42-(2-ethoxyethyl methylphosphonate) (9CI) (CA INDEX NAME)



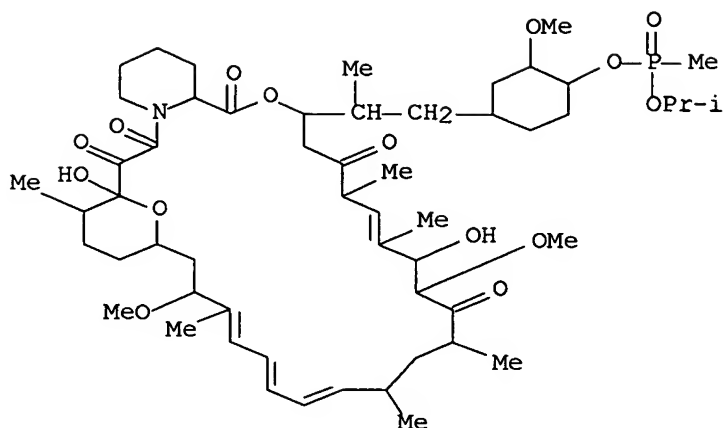
RN 572924-50-6 CAPLUS

CN Rapamycin, 42-(propyl methylphosphonate) (9CI) (CA INDEX NAME)



RN 572924-51-7 CAPLUS

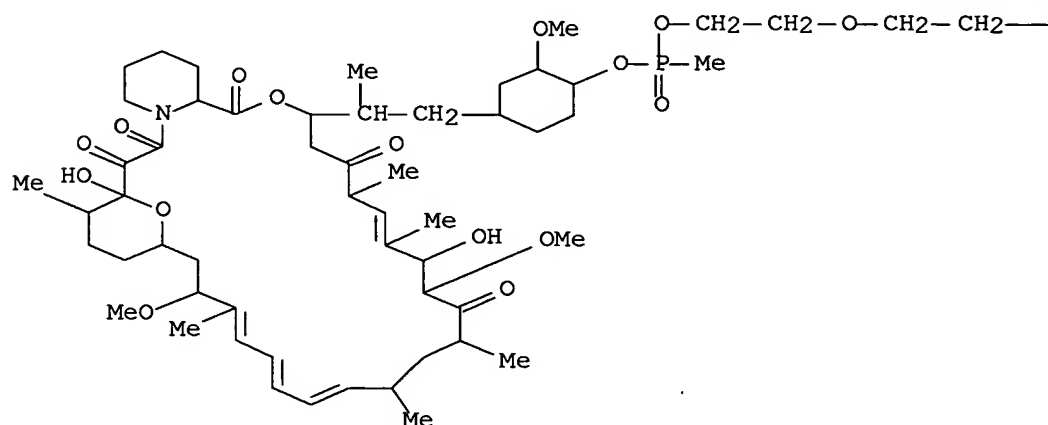
CN Rapamycin, 42-(1-methylethyl methylphosphonate) (9CI) (CA INDEX NAME)



RN 572924-52-8 CAPLUS

CN Rapamycin, 42-[2-(2-hydroxyethoxy)ethyl methylphosphonate] (9CI) (CA INDEX NAME)

PAGE 1-A

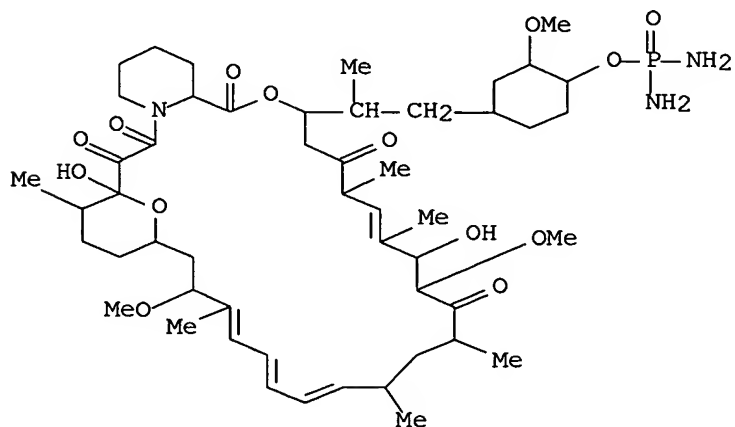


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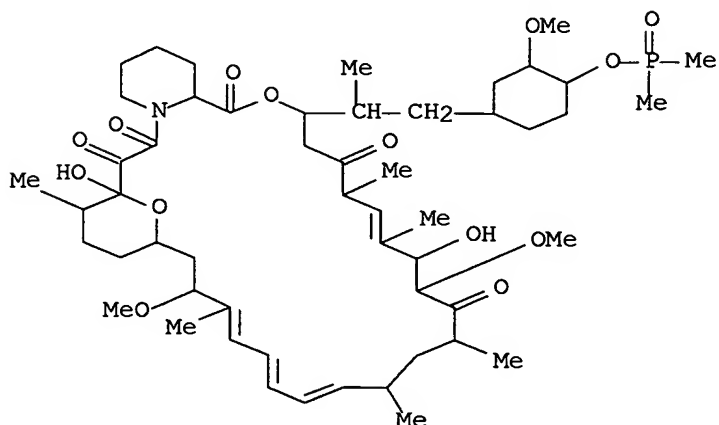
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RN 572924-53-9 CAPLUS

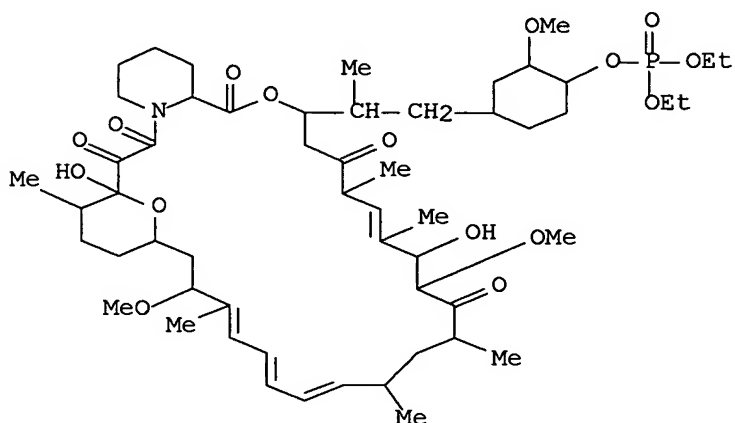
CN Rapamycin, 42-phosphorodiamidate (9CI) (CA INDEX NAME)



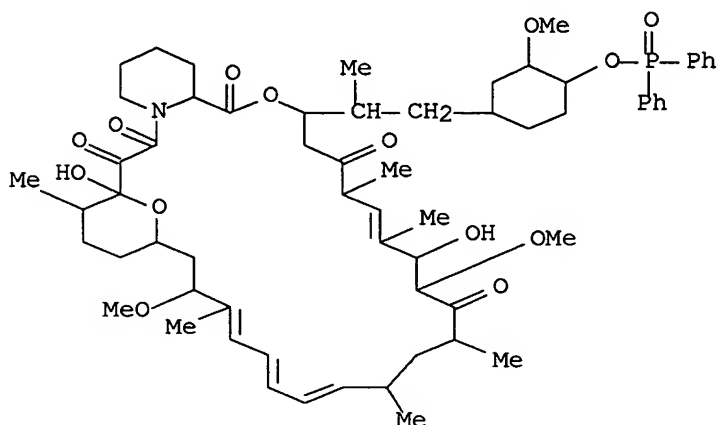
CN    Rapamycin, 42-(dimethylphosphinate) (9CI)    (CA INDEX NAME)



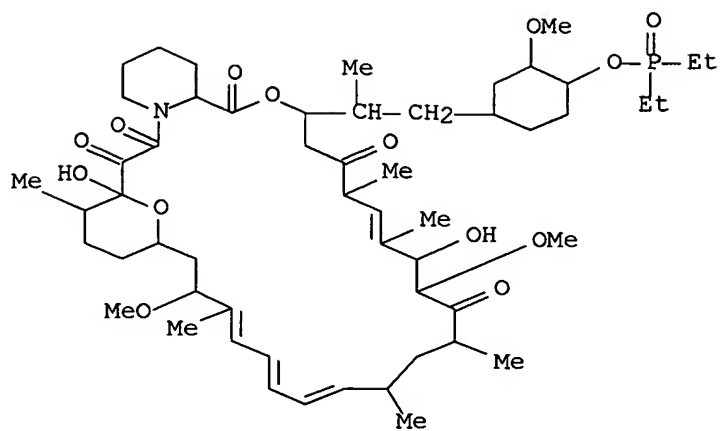
CN Rapamycin, 42-(diethyl phosphate) (9CI) (CA INDEX NAME)



CN	Rapamycin, 42-(diphenyl phosphinate) (9CI)	(CA INDEX NAME)
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CN    Rapamycin, 42-(diethyl phosphinate) (9CI)    (CA INDEX NAME)



L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:610416 CAPLUS Full-text

DN 139:149459

TI Preparation of phosphorus-containing rapamycin derivatives for use in pharmaceutical compositions as immunosuppressive agents

IN Berstein, David L.; Metcalf, Chester A., III; Rozamus, Leonard W.; Wang, Yihan

PA Ariad Gene Therapeutics, Inc., USA

SO PCT Int. Appl., 102 pp.

CODEN: PIXXD2

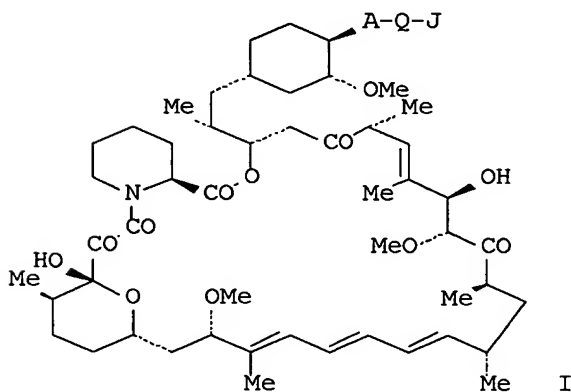
DT Patent

LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003064383	A2	20030807	WO 2003-US3030	20030203
	WO 2003064383	A3	20040122		
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	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	EP 1478648	A2	20041124	EP 2003-735110	20030203
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
	BR 2003007544	A	20041207	BR 2003-7544	20030203
PRAI	US 2002-353252P	P	20020201		
	US 2002-426928P	P	20021115		
	US 2002-428383P	P	20021122		
	US 2002-433930P	P	20021217		
	WO 2003-US3030	W	20030203		
OS	MARPAT 139:149459				

GI



AB Rapamycin derivs. containing a phosphorus moiety, such as I [A = O, S, NR<sub>2</sub>; Q = bond, aliphatic, heteroaliph., aryl, or heteroaryl moiety; J = P(O)(R<sub>5</sub>)<sub>2</sub>, P(O)(R<sub>5</sub>)(OR<sub>5</sub>), P(O)(R<sub>5</sub>)(NR<sub>2</sub>R<sub>5</sub>), P(O)(NR<sub>2</sub>R<sub>5</sub>)<sub>2</sub>, P(O)(OR<sub>5</sub>)(NR<sub>2</sub>R<sub>5</sub>); R<sub>2</sub>, R<sub>5</sub> = H, aliphatic, heteroaliph., heteroaryl,

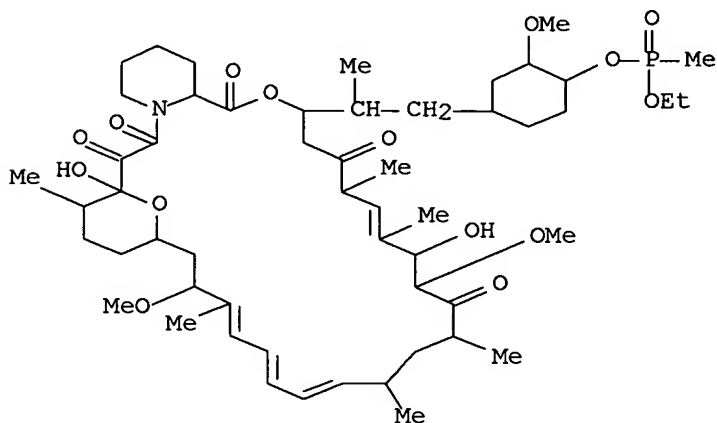
etc.], were prepared for therapeutic use as immunosuppressive agents. These rapamycin derivs. are useful for treatment of graft vs. host disease, lupus, rheumatoid arthritis, diabetes mellitus, myasthenia gravis, multiple sclerosis, psoriasis, dermatitis, eczema, seborrhea, inflammatory bowel disease, pulmonary inflammation, ocular uveitis; adult T-cell leukemia, lymphoma, fungal infections, hyperproliferative restenosis, graft vascular atherosclerosis, coronary artery disease, cerebrovascular disease, arteriosclerosis, atherosclerosis, nonatheromatous arteriosclerosis, or vascular wall damage from cellular events leading toward immune mediated vascular damage, stroke or multi-infarct dementia. Thus, I [A-Q-J = OP(O) (OEt) (Me)] was prepared by reacting rapamycin with Et methylphosphonochloridate using 3,5-lutidine in CH<sub>2</sub>Cl<sub>2</sub> under a nitrogen atmospheric Binding affinity of the rapamycin phosphorus derivs. for human FKBP-12 protein was assayed, dosages for restenosis prevention were discussed.

IT 572924-46-0P 572924-47-1P 572924-48-2P  
 572924-49-3P 572924-50-6P 572924-51-7P  
 572924-52-8P 572924-53-9P 572924-54-0P  
 572924-55-1P 572924-56-2P 572924-57-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of phosphorus-containing rapamycin derivs. for use in pharmaceutical compns. as immunosuppressive agents)

RN 572924-46-0 CAPLUS

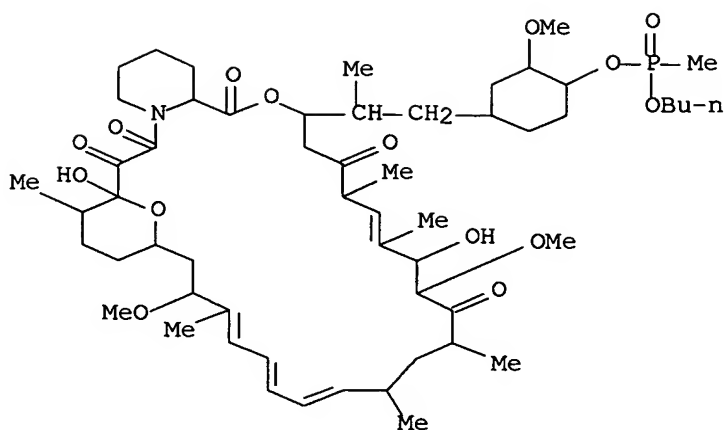
CN Rapamycin, 42-(ethyl methylphosphonate) (9CI) (CA INDEX NAME)



RN 572924-47-1 CAPLUS

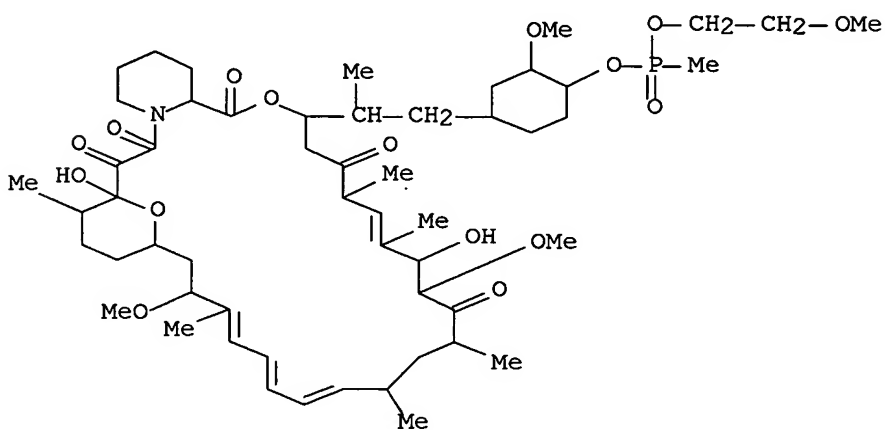
CN Rapamycin, 42-(butyl methylphosphonate) (9CI) (CA INDEX NAME)





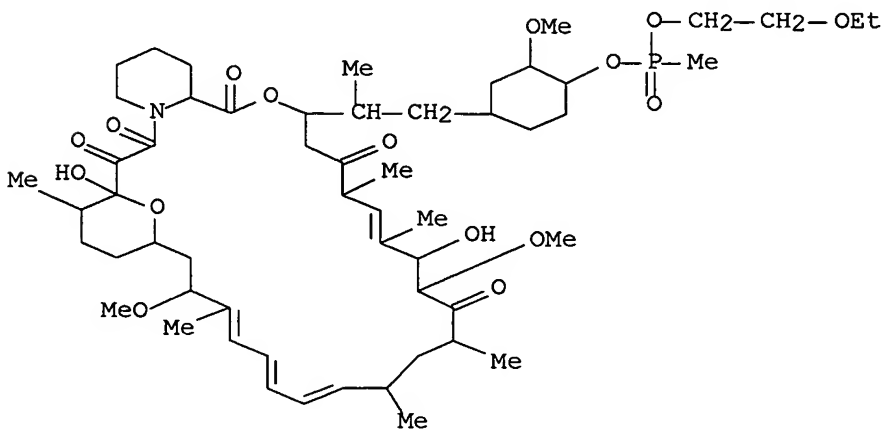
RN 572924-48-2 CAPLUS

CN Rapamycin, 42-(2-methoxyethyl methylphosphonate) (9CI) (CA INDEX NAME)



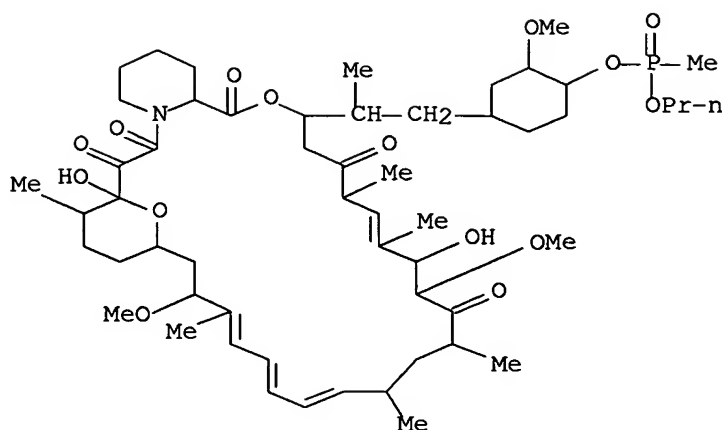
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CN Rapamycin, 42-(2-ethoxyethyl methylphosphonate) (9CI) (CA INDEX NAME)



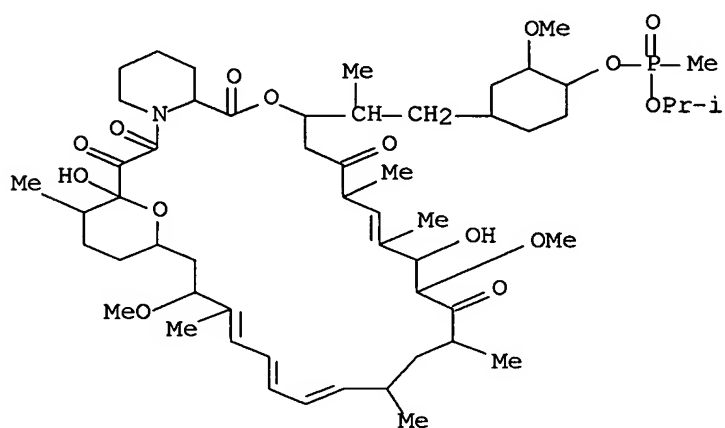
RN 572924-50-6 CAPLUS

CN Rapamycin, 42-(propyl methylphosphonate) (9CI) (CA INDEX NAME)



RN 572924-51-7 CAPLUS

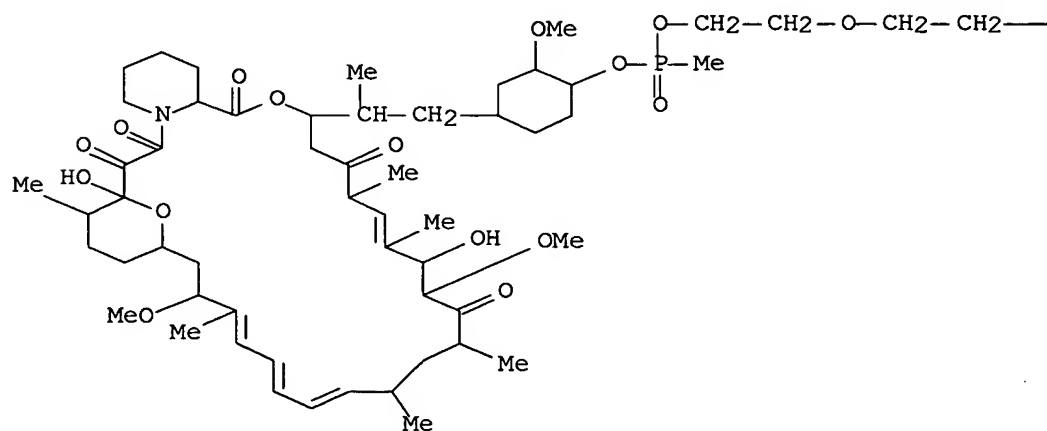
CN Rapamycin, 42-(1-methylethyl methylphosphonate) (9CI) (CA INDEX NAME)



RN 572924-52-8 CAPLUS

CN Rapamycin, 42-[2-(2-hydroxyethoxy)ethyl methylphosphonate] (9CI) (CA INDEX NAME)

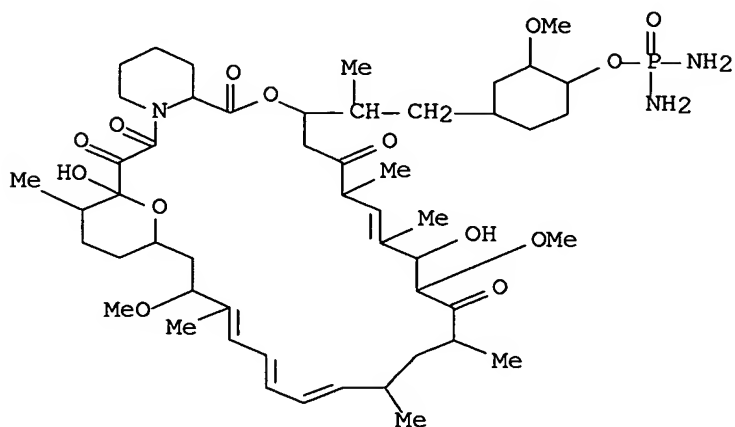
PAGE 1-A



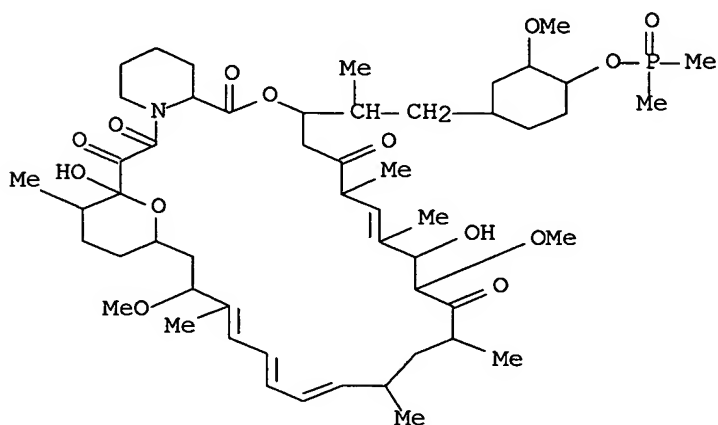
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PAGE 1-B

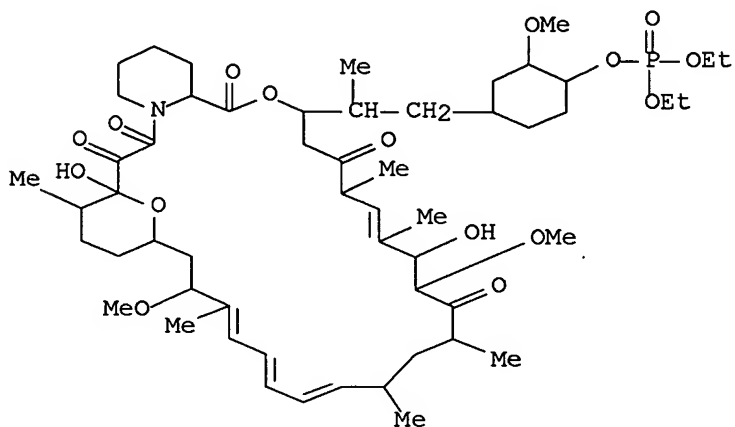
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 CN Rapamycin, 42-phosphorodiamidate (9CI) (CA INDEX NAME)



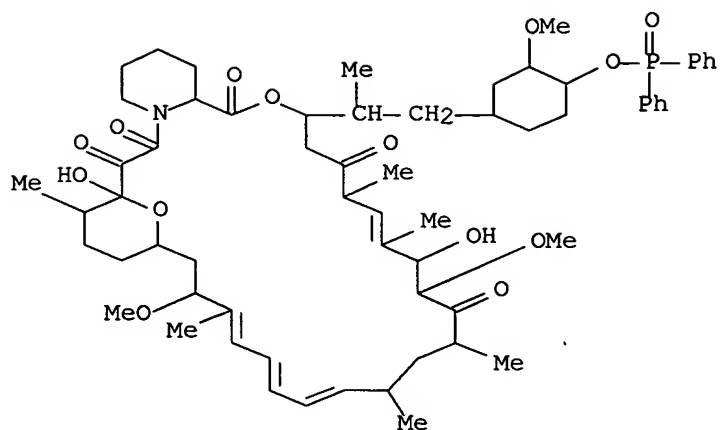
RN 572924-54-0 CAPLUS  
 CN Rapamycin, 42-(dimethylphosphinate) (9CI) (CA INDEX NAME)



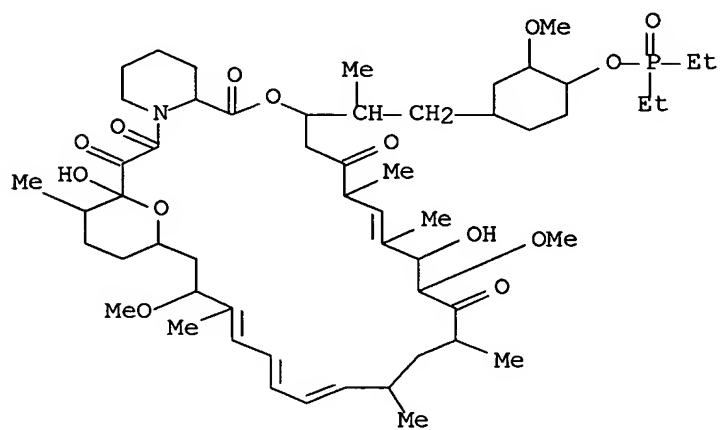
RN 572924-55-1 CAPLUS  
 CN Rapamycin, 42-(diethyl phosphate) (9CI) (CA INDEX NAME)



RN 572924-56-2 CAPLUS  
 CN Rapamycin, 42-(diphenyl phosphinate) (9CI) (CA INDEX NAME)



RN 572924-57-3 CAPLUS  
 CN Rapamycin, 42-(diethyl phosphinate) (9CI) (CA INDEX NAME)



RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1995:605544 CAPLUS Full-text  
 DN 123:9263  
 TI Phosphorylcarbamates of rapamycin and their oxime derivatives  
 IN Skotnicki, Jerauld S.; Smith, Andri L.  
 PA American Home Products Corporation, USA  
 SO U.S., 8 pp.  
 CODEN: USXXAM

DT Patent  
 LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5391730	A	19950221	US 1993-134428	19931008
	US 5455249	A	19951003	US 1994-327335	19941021
PRAI	US 1993-134428	A3	19931008		
OS	MARPAT 123:9263				

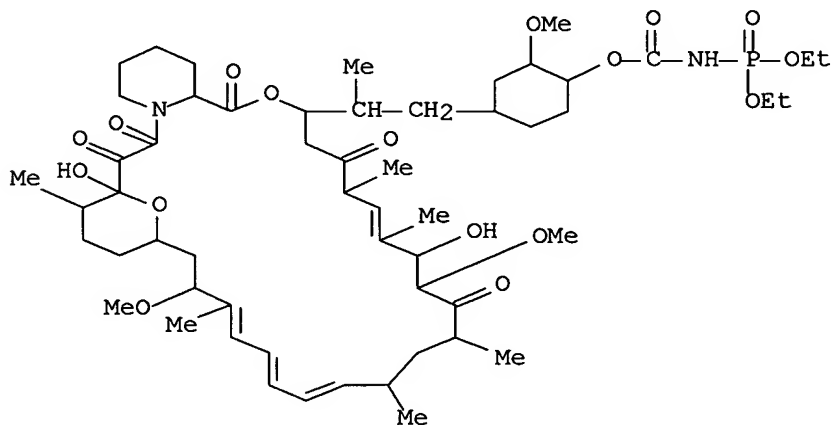
AB 31,42-Diesters and 42-monoesters of rapamycin with phosphinyl isocyanates and their 27-oximes were prepared Thus, rapamycin was treated with 1 equivalent of (EtO)2PNCO to give 36% of the 42-(diethoxyphosphoryl)carbamate which had an IC50 for inhibition of lymphocyte proliferation of 10.0 nM.

IT **163714-67-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (phosphorylcarbamates of rapamycin and their oxime derivs. as immunosuppressants)

RN 163714-67-8 CAPLUS

CN Rapamycin, 42-[(diethoxyphosphinyl)carbamate] (9CI) (CA INDEX NAME)



L4 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1993:146230 CAPLUS Full-text

DN 118:146230

TI Process for biophosphorylating organic compounds

IN Chen, Shieh Shung Tom; Petuch, Brian R.; Hsu, Annjia T.; Arison, Byron H.; Dumont, Francis; White, Raymond F.; Mathre, David J.; Wu, Jane T.; So, Lydia T.; Reamer, Robert A.

PA Merck and Co., Inc., USA

SO PCT Int. Appl., 159 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 9206992	A2	19920430	WO 1991-US6816	19910919
	WO 9206992	A3	19920625		
	W: CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	US 5198421	A	19930330	US 1991-691606	19910426
	CA 2093429	AA	19920410	CA 1991-2093429	19910919
	EP 552309	A1	19930728	EP 1992-901105	19910919
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 06502536	T2	19940324	JP 1992-501234	19910919
PRAI	US 1990-594214	A2	19901009		
	US 1990-594500	A	19901009		
	US 1990-595894	A	19901011		
	US 1991-691606	A	19910426		
	US 1991-691607	A	19910426		
	US 1991-701387	A	19910516		
	US 1991-735963	A	19910725		
	WO 1991-US6816	W	19910919		

AB Phosphorylated organic compds. are prepared by incubating the hydroxyl-containing organic compds. such as FK506-type macrolides with *Rhizopus oryzae*, or echinocandins with *R. arrhizus*. By this process inflammation inhibitors, HIV protease inhibitors, and compds. with immunoregulatory activity can be prepared C-32 phosphorylated FK-506 was prepared from FK-506 with *R. oryzae* and tested for its ability to inhibit T cell proliferation. The organic synthesis of various bioactive compds., their biophosphorylation and testing for biol. activity, and formulation are described.

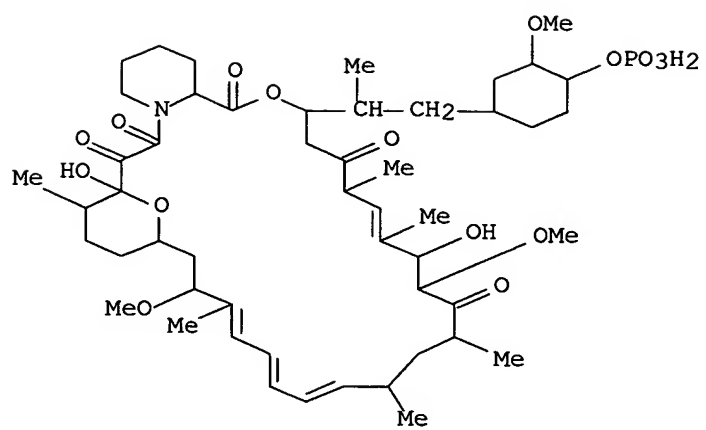
IT **143715-59-7P**

RL: PREP (Preparation)

(preparation of, by biophosphorylation with *Rhizopus oryzae*)

RN 143715-59-7 CAPLUS

CN Rapamycin, 42-phosphate (9CI) (CA INDEX NAME)





L8 ANSWER 1 OF 15 MARPAT COPYRIGHT 2005 ACS on STN  
 AN 124:250930 MARPAT Full-text  
 TI Hindered N-oxide esters of rapamycin  
 IN Nelson, Frances C.; Schiehser, Guy A.  
 PA American Home Products Corporation, USA  
 SO U.S., 7 pp.  
 CODEN: USXXAM

DT Patent  
 LA English

FAN.CNT 1

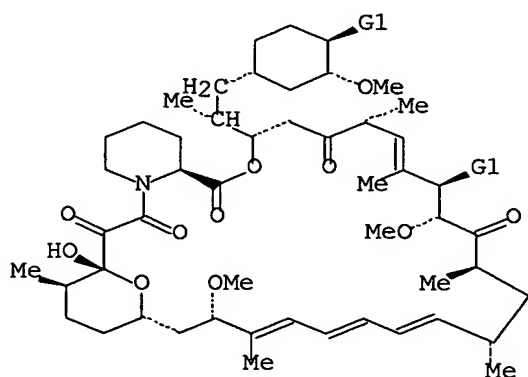
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PI	US 5491231	A	19960213	US 1994-345972	19941128
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	US 5508285	A	19960416	US 1995-449168	19950524
	US 5521194	A	19960528	US 1995-450769	19950524
	US 5559122	A	19960924	US 1995-448843	19950524
	CA 2205577	AA	19960606	CA 1995-2205577	19951122
	WO 9616967	A1	19960606	WO 1995-US15318	19951122
	W: AL, AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, UZ, VN				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9642877	A1	19960619	AU 1996-42877	19951122
	AU 712998	B2	19991118		
	EP 794955	A1	19970917	EP 1995-941467	19951122
	EP 794955	B1	20010725		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	BR 9509825	A	19970930	BR 1995-9825	19951122
	HU 77139	A2	19980302	HU 1997-1851	19951122
	JP 10509977	T2	19980929	JP 1995-518953	19951122
	NZ 297661	A	20000128	NZ 1995-297661	19951122
	AT 203539	E	20010815	AT 1995-941467	19951122
	ES 2158959	T3	20010916	ES 1995-941467	19951122
	PT 794955	T	20011228	PT 1995-941467	19951122
	FI 9702240	A	19970527	FI 1997-2240	19970527
	HK 1002281	A1	20011102	HK 1998-101292	19980219
	GR 3036712	T3	20011231	GR 2001-401569	20010926
PRAI	US 1994-345972		19941128		
	WO 1995-US15318		19951122		
GI					

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB A compound I is disclosed [R, R1 = C(O)(CH2)kC(R2)(R3)(CH2)nR4, C(O)(CH2)mC(R5)(R6)R7, H; R2, R3 = alkyl, arylalkyl, or R2 and R3 may be taken together to form cycloalkyl ring; R4 = (optionally substituted) heterocyclic N-oxide radical; R5 = alkyl, arylalkyl; R6 and R7 together form (optionally substituted) saturated N-alkyl heterocyclic N-oxide; k = 0, 1, m = 0, 1; n = 1-6; with the proviso that R and R1 are not both hydrogen], which is useful as an immunosuppressive, antiinflammatory, antifungal, antiproliferative, and antitumor agent. Preparation of

rapamycin 42-ester with 2,2-dimethyl-3-(3-pyridinyl) propionic acid N-oxide is described; the compound was tested in e.g. a standard procedure measuring lymphocyte proliferation as a measure of the immunosuppressive effect.

**MSTR 1A**



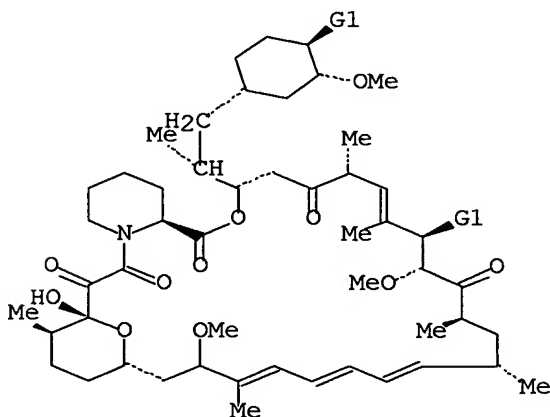
G1 = (-1) OH  
 G10 = PO3H2  
 MPL: claim 1  
 NTE: substitution is restricted  
 NTE: also incorporates broader disclosure

L8 ANSWER 2 OF 15 MARPAT COPYRIGHT 2005 ACS on STN  
 AN 124:175686 MARPAT Full-text  
 TI Carbamates of rapamycin  
 IN Kao, Wenling; Abou-Gharbia, Magid A.; Vogel, Robert L.  
 PA American Home Products Corporation, USA  
 SO U.S., 16 pp. Cont.-in-part of U.S. Ser. No. 160,984, abandoned.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5480989	A	19960102	US 1994-297663	19940901
	US 5302584	A	19940412	US 1993-54655	19930423
	US 5530007	A	19960625	US 1995-402590	19950313
	US 5559120	A	19960924	US 1995-402571	19950313
	US 5508399	A	19960416	US 1995-450835	19950525
	US 5530121	A	19960625	US 1995-451104	19950525
PRAI	US 1992-960597	19921013			
	US 1993-54655	19930423			
	US 1993-160984	19931201			
	US 1994-297663	19940901			

AB Rapamycin 42-carbamates with aminoalkanes and nitrogen heterocycles (>50 compds.) were prepared as immunosuppressants. Thus, rapamycin was esterified by ClCO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>(NO<sub>2</sub>)-4 and this carbonate amidated with N,N-diethylethylenediamine to give rapamycin 42-(2-diethylaminoethyl)carbamate (I). I.HCl salt was evaluated for immunosuppressive activity in in vivo pinch skin graft and showed a survival time of 13.6 days at 4 mg/kg vs. controls which were 6-7 days.

#### MSTR 1



G1 = (-1) OH

G13 = 145

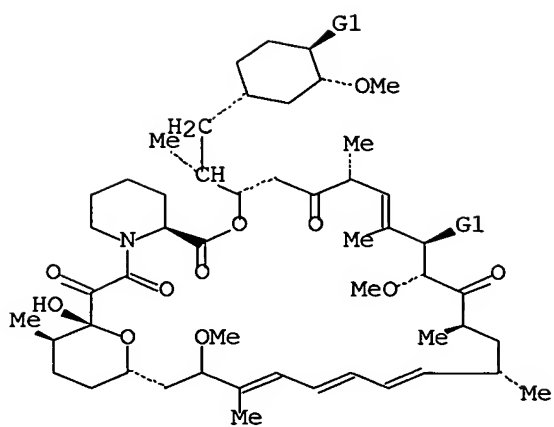
<sup>145</sup>P-H

DER: or pharmaceutically acceptable salts

MPL: claim 1

NTE: substitution is restricted

#### MSTR 2



G1 = (-1) OH  
 G13 = 145

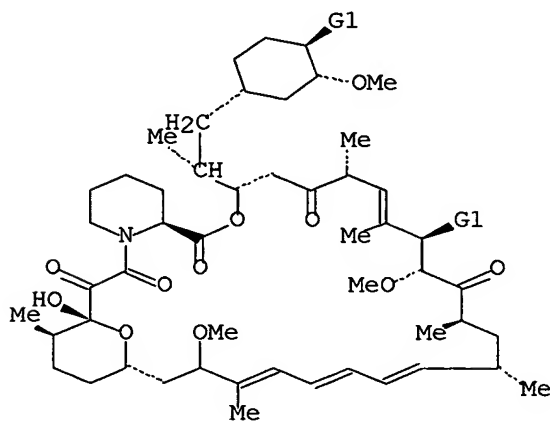
$^{145}_{145} \text{H}$

DER: or pharmaceutically acceptable salts  
 MPL: disclosure

L8 ANSWER 3 OF 15 MARPAT COPYRIGHT 2005 ACS on STN  
 AN 124:145748 MARPAT Full-text  
 TI Carbamates of rapamycin  
 IN Failli, Amedeo A.; Bleyman, Oleg I.; Kao, Wenling; Abou-Gharbia, Magid A.  
 PA American Home Products Corporation, USA  
 SO U.S., 13 pp. Cont.-in-part of U.S. Ser. No. 160,984, abandoned.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5480988	A	19960102	US 1994-284764	19940802
	US 5302584	A	19940412	US 1993-54655	19930423
	US 5486522	A	19960123	US 1995-448709	19950524
	US 5486524	A	19960123	US 1995-449166	19950524
	US 5486523	A	19960123	US 1995-449444	19950524
	US 5504204	A	19960402	US 1995-449453	19950524
	US 5550133	A	19960827	US 1995-448869	19950524
	US 5559227	A	19960924	US 1995-449593	19950524
PRAI	US 1992-960597		19921013		
	US 1993-54655		19930423		
	US 1993-160984		19931201		
	US 1994-284764		19940802		
AB	Rapamycin 42-carbamates with alkyn- and alkenamines (10 compds.) were prepared and tested for immunosuppressant and antiinflammatory activity. Thus, rapamycin was esterified by ClCO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> (NO <sub>2</sub> )-4 and this carbonate amidated with 3-(N-methyl-N-prop-2-ynylamino)propylamine to give rapamycin 42-[3-(N-methyl-N-prop-2-ynylamino)propyl] carbamate (I). I-methanesulfonate was evaluated for immunosuppressive activity in in vivo pinch skin graft and showed a survival time of 11.0 days at 4 mg/kg vs. controls which were 6-7 days. In adjuvant arthritis standard pharmacol. test I-methane sulfonate demonstrated better activity than rapamycin in treating or inhibiting rheumatoid arthritis.				

## MSTR 2



G1 = (-1) OH  
 G13 = 145

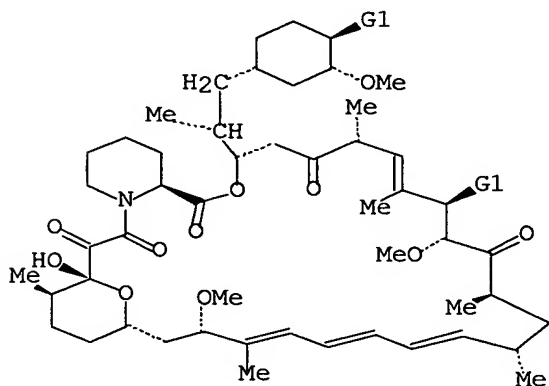
145-H

L8 ANSWER 4 OF 15 MARPAT COPYRIGHT 2005 ACS on STN  
 AN 123:285648 MARPAT Full-text  
 TI Carbamates of rapamycin  
 IN Skotnicki, Jerauld S.; Palmer, Yvette L.; Kao, Wenling; Abou-Gharbia, Magid A.  
 PA American Home Products Corporation, USA  
 SO U.S., 9 pp. Cont.-in-part of U.S. Ser. No. 160,984, abandoned.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5434260	A	19950718	US 1994-259701	19940614
	US 5302584	A	19940412	US 1993-54655	19930423
	US 5516780	A	19960514	US 1995-391400	19950227
	US 5519031	A	19960521	US 1995-391398	19950227
	US 5532355	A	19960702	US 1995-395012	19950227
	US 5559119	A	19960924	US 1995-391399	19950227
	US 5559112	A	19960924	US 1995-395402	19950227
	US 5567709	A	19961022	US 1995-395013	19950227
PRAI	US 1992-960597	19921013			
	US 1993-54655	19930423			
	US 1993-160984	19931201			
	US 1994-259701	19940614			

AB 42-O-esters of heterocyclic carbamic acids were prepared Thus, rapamycin was converted to its 42-O-(4-nitrophenoxy carbonyl) derivative which was treated with 5-phenyl-1,4,5,6-tetrahydropyrimidine hydrochloride to give the rapamycin 42-O-ester with 5-phenyl-1,4,5,6-tetrahydropyrimidine-1- carboxylic acid. The latter compound had an immunosuppressive IC50 of 0.54 nM in the test using BAB/c donor skin grafts in C2H(H-2K) mice.

## MSTR 2



G1 = (-1) OH  
 G6 = 126

126—G15

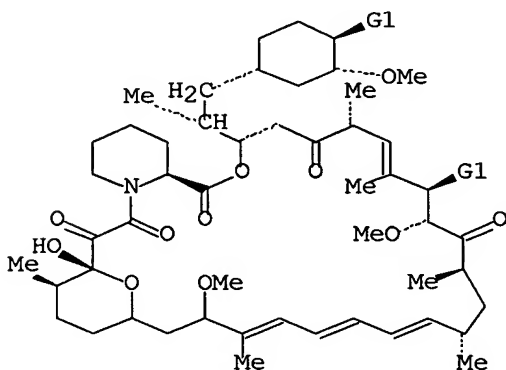
DER: or pharmaceutically acceptable salts  
 MPL: disclosure  
 NTE: alkylene in G14 may be interrupted

L8 ANSWER 5 OF 15 MARPAT COPYRIGHT 2005 ACS on STN  
 AN 123:83100 MARPAT Full-text  
 TI Carbamates of rapamycin  
 IN Kao, Wenling; Skotnicki, Jerauld S.; Abou-Gharbia, Magid A.; Palmer, Yvette L.  
 PA American Home Products Corporation, USA  
 SO U.S., 25 pp. Cont.-in-part of U.S. Ser. No. 160,984, abandoned.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5411967	A	19950502	US 1994-224893	19940408
	US 5302584	A	19940412	US 1993-54655	19930423
PRAI	US 1992-960597	19921013			
	US 1993-54655	19930423			
	US 1993-160984	19931201			

AB 42- And/or 31-esters of rapamycin with carbamic acids are useful as immunosuppressive, antiinflammatory, antifungal, antiproliferative, and antitumor agents. Thus, rapamycin was treated with 4-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>O<sub>2</sub>CCl to give the 42-p-nitrophenyl carbonate which was treated with NH<sub>3</sub> to give the 42-carbamate. The latter compound had an IC<sub>50</sub> in the lymphocyte proliferation test of 1.7 nM.

## MSTR 2



G1 = OH  
 G4 = 73

7<sup>B</sup>—H

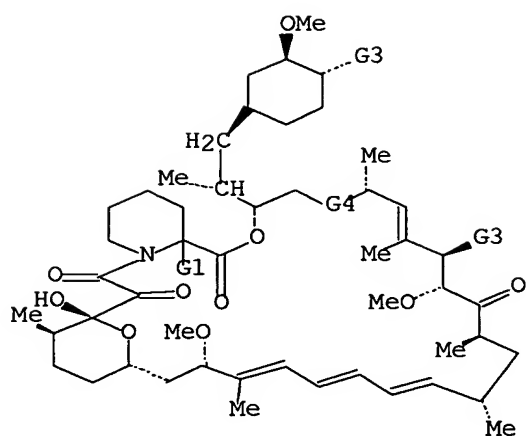
DER: or pharmaceutically acceptable salts  
 MPL: disclosure  
 NTE: substitution is restricted

L8 ANSWER 6 OF 15 MARPAT COPYRIGHT 2005 ACS on STN  
 AN 122:314360 MARPAT Full-text  
 TI C-22 ring stabilized rapamycin derivatives  
 IN Nelson, Frances C.  
 PA American Home Products Corp., USA  
 SO U.S., 22 pp.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5387680	A	19950207	US 1993-105090	19930810
	CA 2169277	AA	19950216	CA 1994-2169277	19940810
	WO 9504738	A1	19950216	WO 1994-US9041	19940810
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, UZ, VN				
	RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9475601	A1	19950228	AU 1994-75601	19940810
	AU 676086	B2	19970227		
	EP 713490	A1	19960529	EP 1994-925809	19940810
	EP 713490	B1	19980225		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	BR 9407236	A	19960924	BR 1994-7236	19940810
	CN 1132512	A	19961002	CN 1994-193603	19940810
	HU 74675	A2	19970128	HU 1996-298	19940810
	JP 09501436	T2	19970210	JP 1995-506598	19940810
	AT 163420	E	19980315	AT 1994-925809	19940810
	ES 2115255	T3	19980616	ES 1994-925809	19940810
	PL 178625	B1	20000531	PL 1994-312991	19940810
	RU 2152946	C1	20000720	RU 1996-107113	19940810
	CZ 291205	B6	20030115	CZ 1996-358	19940810
PRAI	US 1993-105090		19930810		
	WO 1994-US9041		19940810		
OS	CASREACT 122:314360				
AB	This invention provides C-22 substituted rapamycin derivs. and pharmaceutically acceptable salts thereof which are useful for inducing immunosuppression.				

MSTR 1

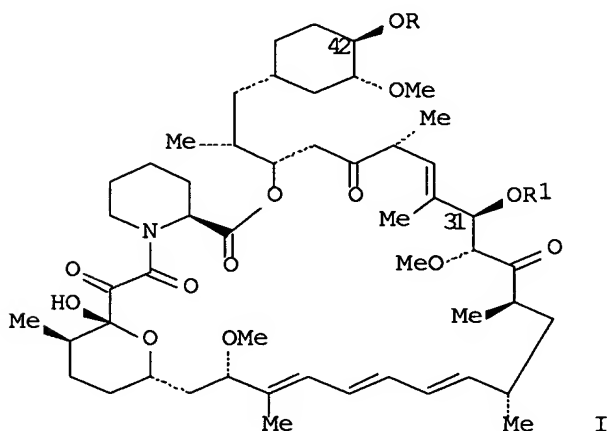




G3 = OH  
 G4 = C(O)  
 G13 = PO3H2  
 DER: or pharmaceutically acceptable salts  
 MPL: claim 6  
 NTE: substitution is restricted

L8 ANSWER 7 OF 15 MARPAT COPYRIGHT 2005 ACS on STN  
 AN 122:265180 MARPAT Full-text  
 TI Immunosuppressant gem-disubstituted esters of rapamycin  
 IN Ocain, Timothy D.; Schiehser, Guy A.  
 PA American Home Products Corp., USA  
 SO U.S., 14 pp.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 FAN.CNT 1

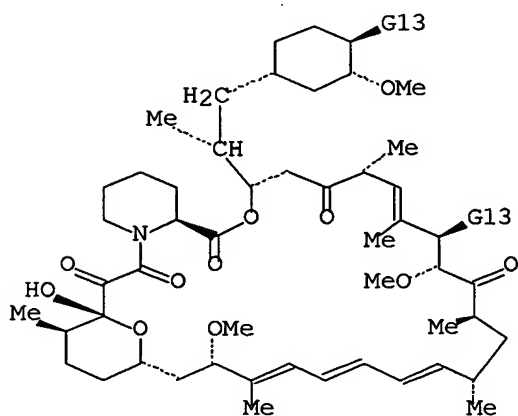
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5385910	A	19950131	US 1993-156334	19931122
PRAI	US 1993-156334		19931122		
GI					



AB A compound of the structure I wherein R and R1 are each, independently, hydrogen, or CO(CH<sub>2</sub>)<sub>m</sub>CR<sub>2</sub>R<sub>3</sub>(CH<sub>2</sub>)<sub>n</sub>NR<sub>4</sub>R<sub>5</sub>; R<sub>2</sub> and R<sub>3</sub> are each, independently, alkyl of 1-6 carbon atoms, arylalkyl of 7-10 carbon atoms, or may be taken together to form a cycloalkyl ring of 3-8 carbon atoms; R<sub>4</sub> and R<sub>5</sub> are each, independently, hydrogen, alkyl of 1-6 carbon atoms, arylalkyl of 7-10 carbon atoms, or may be taken together to form a saturated heterocycle having 3-6 carbon atoms selected from the group consisting of piperidine, morpholine, thiomorpholine, piperazine, pyrazolidine, imidazolidine, and pyrrolidine, wherein the heterocyclic ring may be optionally mono-, di-, or tri-substituted with a group selected from alkyl of 1-6 carbon atoms and perfluoroalkyl of 1-6 carbon atoms; wherein the aryl moiety of the arylalkyl group of R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, and R<sub>5</sub> is, e.g., Ph, naphthyl, pyridinyl; m=0-1; and n=0-6; with the proviso that R and R1 are not both hydrogen, or a pharmaceutically acceptable salt thereof which is useful as an immunosuppressive, antiinflammatory, antifungal, antiproliferative, and antitumor agent. Immunosuppressive activity for representative compds. of this invention was evaluated in an in vitro standard pharmacol. test procedure to measure lymphocyte

proliferation (LAF) and in three in vivo standard pharmacol. test procedures. Thus, e.g., for rapamycin 42-ester with 2-amino-2-methylpropionic acid maleate salt, LAF IC50 : 5.3 and 8.4 nM; skin graft survival time:  $12.0 \pm 0.0$  and  $11.0 \pm 0.9$  days; percent change in adjuvant arthritis vs. control: -73%; heart allograft survival time: 19.11 days. Pharmaceutical formulations were given.

# **MSTR 1**



G6 = PO3H2  
 G13 = (-1) OH  
 DER: and pharmaceutically acceptable salts  
 MPL: claim 1  
 NTE: includes broader disclosure

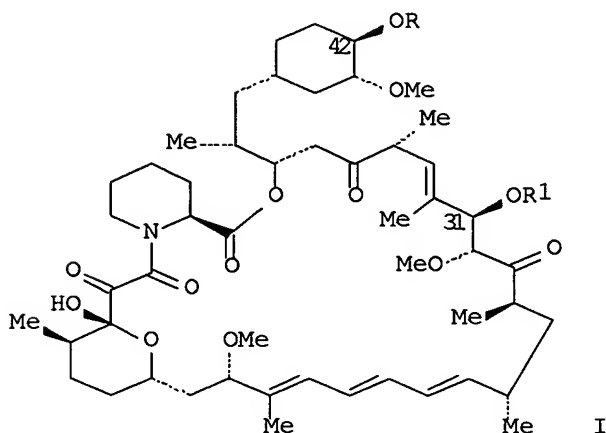
L8 ANSWER 8 OF 15 MARPAT COPYRIGHT 2005 ACS on STN  
 AN 122:265179 MARPAT Full-text  
 TI Heterocyclic esters of rapamycin  
 IN Nelson, Frances C.; Schiehser, Guy A.  
 PA American Home Products Corp., USA  
 SO U.S., 11 pp.  
 CODEN: USXXAM

DT Patent  
 LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5385909	A	19950131	US 1993-156208	19931122
	CA 2176961	AA	19950601	CA 1994-2176961	19941116
	WO 9514697	A1	19950601	WO 1994-US13411	19941116
	W:	AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, UZ, VN			
	RW:	KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	AU 9510571	A1	19950613	AU 1995-10571	19941116
	EP 730597	A1	19960911	EP 1995-901258	19941116
	EP 730597	B1	20010307		
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE			
	JP 09505596	T2	19970603	JP 1994-515166	19941116
	AT 199555	E	20010315	AT 1995-901258	19941116
	ES 2154720	T3	20010416	ES 1995-901258	19941116
	PT 730597	T	20010629	PT 1995-901258	19941116
	HK 1011354	A1	20010622	HK 1998-112278	19981124
	GR 3035835	T3	20010831	GR 2001-400683	20010507
PRAI	US 1993-156208		19931122		
	WO 1994-US13411		19941116		

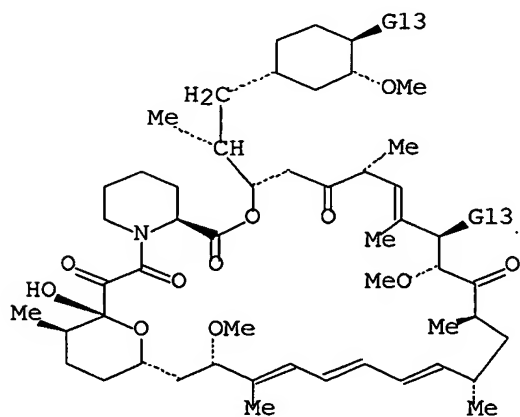
GI



AB A compound of the structure I wherein R and R1 are each, independently, CO(CH<sub>2</sub>)<sub>n</sub>R<sub>2</sub> or hydrogen, R<sub>2</sub> is a heterocyclic radical which may be optionally substituted; n=0-6; with the proviso that R and R1 are both not hydrogen, or a pharmaceutically acceptable salt thereof which is useful as an immunosuppressive, antiinflammatory, antifungal, antiproliferative, and antitumor agent. Immunosuppressive activity for representative compds. of this invention was evaluated in an in vitro

standard pharmacol. test procedure to measure lymphocyte proliferation (LAF) and in three in vivo standard pharmacol. test procedures. Thus, e.g., for rapamycin 42-ester with 2-methylnicotinic acid: LAF IC50 = 1.00 nM; skin graft survival: 11.2 ± 0.8 days; percent change in adjuvant arthritis vs. control: -88%; heart allograft survival: 29.9 days, i.p. Pharmaceutical formulations were given.

**MSTR 1**

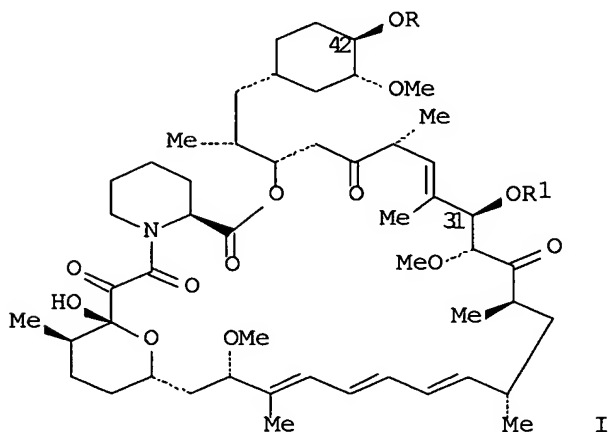


G6 = PO3H2  
 G13 = (-1) OH  
 DER: and pharmaceutically acceptable salts  
 MPL: claim 1  
 NTE: includes broader disclosure

I8 ANSWER 9 OF 15 MARPAT COPYRIGHT 2005 ACS on STN  
 AN 122:265178 MARPAT Full-text  
 TI Immunosuppressant hindered esters of rapamycin  
 IN Nelson, Frances C.; Schiehser, Guy A.  
 PA American Home Products Corp., USA  
 SO U.S., 16 pp.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5385908	A	19950131	US 1993-156206	19931122
	CA 2176955	AA	19950601	CA 1994-2176955	19941118
	WO 9514696	A1	19950601	WO 1994-US13310	19941118
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, UZ, VN RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9512575	A1	19950613	AU 1995-12575	19941118
	EP 730598	A1	19960911	EP 1995-903559	19941118
	EP 730598	B1	19990609		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	JP 09505592	T2	19970603	JP 1994-515148	19941118
	AT 181076	E	19990615	AT 1995-903559	19941118
	ES 2133715	T3	19990916	ES 1995-903559	19941118
	SG 80525	A1	20010522	SG 1996-2897	19941118
	HK 1013063	A1	20000428	HK 1998-112277	19981124
PRAI	US 1993-156206		19931122		
	WO 1994-US13310		19941118		

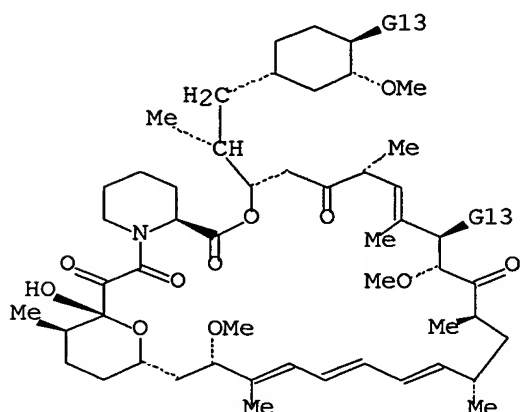
GI



AB A compound of the structure I wherein R and R1 are each, independently, CO(CH2)kCR2R3(CH2)nR4, CO(CH2)mCR3R5R6, or hydrogen; R2 and R3 are each, independently, alkyl, arylalkyl, or R2 and R3 may be taken together to form a cycloalkyl ring; R4 is a heterocyclic radical which may be optionally substituted; R5 is alkyl or arylalkyl; R6 and R7 are taken together to form a saturated heterocyclic ring which may be optionally substituted; k=0-1, m=0-1; n=1-6; with the proviso that R and R1 are not both hydrogen, or a pharmaceutically acceptable salt thereof, which is

useful as an immunosuppressive, antiinflammatory, antifungal, antiproliferative, and antitumor agent. Immunosuppressive activity for representative compds. of this invention was evaluated in an in vitro standard pharmacol. test procedure to measure lymphocyte proliferation (LAF) and in three in vivo standard pharmacol. test procedures. Thus, e.g., for rapamycin 42-ester with 2,2-dimethyl-3-(3-pyridinyl) propionic acid, LAF IC50: 0.83 nM; skin graft survival:  $13.6 \pm 0.6$  days; percent change in adjuvant arthritis vs. control: -62%; heart allograft: 29 days, i.p.; 11.5 days, p.o. Pharmaceutical formulations were given. Safety note: authors identify 3-picolyl chloride as a lachrymator.

# **MSTR 1**

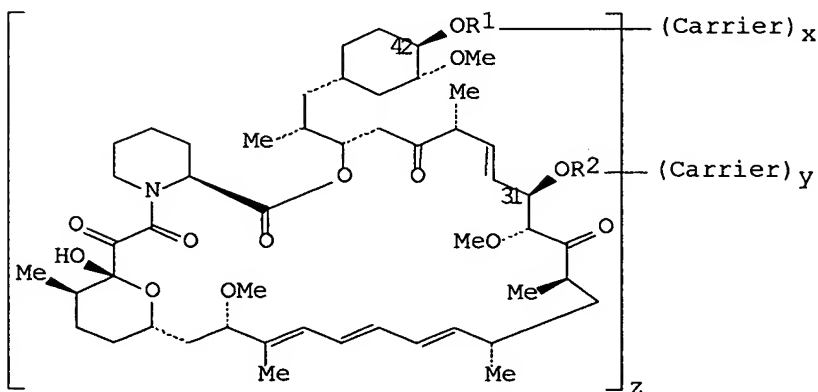


G6 = PO3H2  
 G13 = (-1) OH  
 DER: and pharmaceutically acceptable salts  
 MPL: claim 1  
 NTE: includes broader disclosure

L8 ANSWER 10 OF 15 MARPAT COPYRIGHT 2005 ACS on STN  
 AN 122:213858 MARPAT Full-text  
 TI Preparation of rapamycin conjugates for generation of antibodies  
 IN Molnar-Kimber, Katherine Lu; Ocain, Timothy Donald; Caufield, Craig Eugene; Caggiano, Thomas Joseph; Failli, Amedeo Arturo  
 PA American Home Products Corp., USA  
 SO PCT Int. Appl., 42 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9425072	A1	19941110	WO 1994-US4463	19940422
	W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, UZ, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9467119	A1	19941121	AU 1994-67119	19940422
	EP 1181938	A2	20020227	EP 2001-120777	19940422
	EP 1181938	A3	20020320		
	R: BE, CH, DE, ES, FR, GB, IT, LI				
	US 6328970	B1	20011211	US 2000-576952	20000524
	US 2001010920	A1	20010802	US 2001-773562	20010202
	US 6541612	B2	20030401		
	US 2002151088	A1	20021017	US 2002-124386	20020418
	JP 2004149542	A2	20040527	JP 2003-412072	20031210
	JP 2004168782	A2	20040617	JP 2003-412071	20031210
PRAI	US 1993-53030		19930423		
	US 1994-224207		19940414		
	US 1994-224205		19940414		
	EP 1994-915854		19940422		
	JP 1994-524408		19940422		
	WO 1994-US4463		19940422		
	US 1995-424983		19950419		
	US 2000-576951		20000524		
	US 2000-576952		20000524		

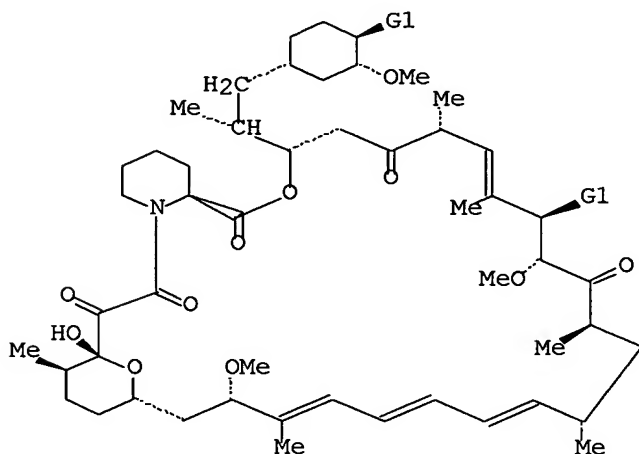
GI



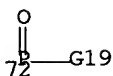


AB Title compds. I [(R1, R2 = H, (R3LR4) wherein L = linking group, R3 = CO, SO, SO2, PO2, POME,CS, CH2CO; R4 = CO, NH, S, CH2, O; a = 1-5; z = 1-120), carrier = immunogenic material, detector material, solid matrix, salt; x, y = 0,1 with provisos], are prepared Succinic anhydride and dimethylaminopyridine were added to II to give II 42-ester with succinic acid which was treated with N-hydroxysuccinimide to give II 42-ester with N-hydroxysuccinimide hemisuccinate which was conjugated with proteins and horseradish peroxidase. Screening for monoclonal antibodies specific for II or its derivs. as well as immunoassay are given.

# **MSTR 1**



G1 = (-1) OH  
G3 = 72

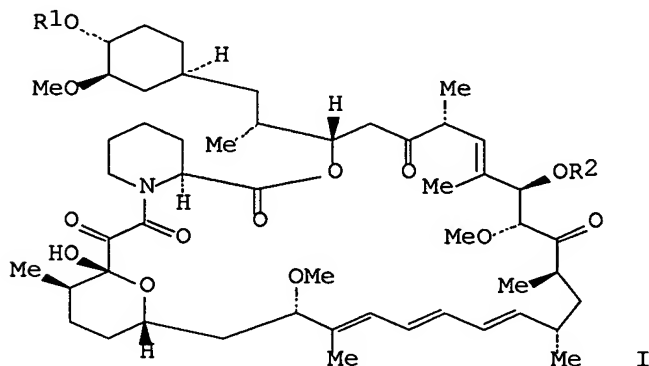


DER: or salts  
MPL: claim 1

L8 ANSWER 11 OF 15 MARPAT COPYRIGHT 2005 ACS on STN  
 AN 121:179406 MARPAT Full-text  
 TI Preparation of O-(imidazolylalkyl)rapamycins and analogs as  
 immunosuppressants and antimicrobials  
 IN Goulet, Mark; Parsons, William H.; Wyvratt, Matthew J.  
 PA Merck and Co., Inc., USA  
 SO U.S., 35 pp.  
 CODEN: USXXAM

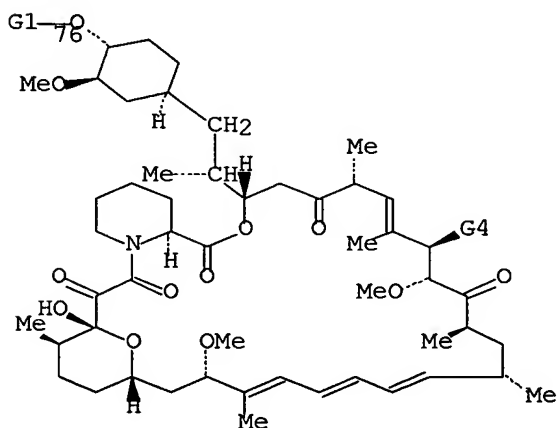
DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5310903	A	19940510	US 1993-26925	19930305
PRAI	US 1993-26925		19930305		
GI					



AB Title compds. [I; R1 = (un)substituted 2-imidazolylmethyl, -benzyl, etc.; R2 = H, groups cited for R1, etc.] were prepared as immunosuppressants and antimicrobials (no data). Thus, rapamycin was converted in 3 steps to 42-(2-oxoethoxy)rapamycin which was cyclocondensed with phenylglyoxal and NH3 to give 42-[(4-phenyl-2-imidazolyl)methoxy]rapamycin.

#### MSTR 1

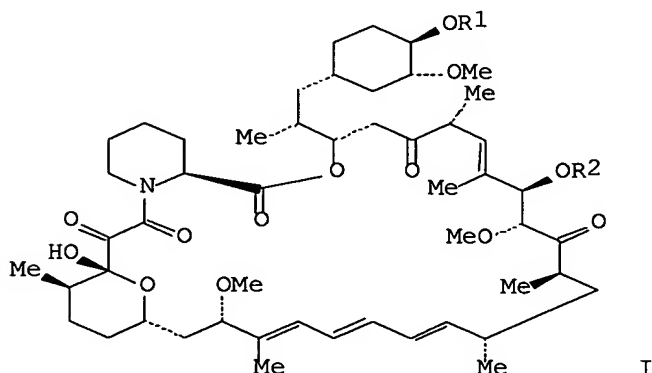


G4 = OH  
 G7 = PO3H2  
 DER: or pharmaceutically acceptable salts

MPL: claim 1  
NTE: Ak in G16 and alkylene in G17 may be optionally interrupted

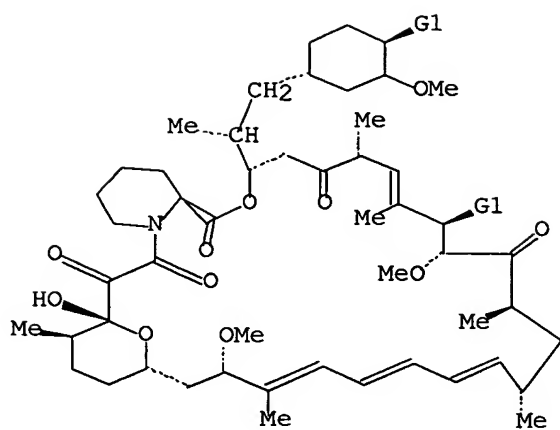
L8 ANSWER 12 OF 15 MARPAT COPYRIGHT 2005 ACS on STN  
 AN 121:108376 MARPAT Full-text  
 TI Preparation of rapamycin carbamates  
 IN Kao, Wenling; Abou-Gharbia, Magid Abdel; Vogel, Robert Lewis  
 PA American Home Products Corp., USA  
 SO Eur. Pat. Appl., 26 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 593227	A1	19940420	EP 1993-308040	19931008
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	US 5302584	A	19940412	US 1993-54655	19930423
	EP 1266900	A1	20021218	EP 2002-14573	19931008
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
PRAI	US 1992-960597		19921013		
	US 1993-54655		19930423		
	GB 1993-17596		19930824		
	EP 1993-308040		19931008		
GI					



AB Title compds. I (R1, R2 = H, -CONH-[(CR3R4)m(-A-(CR5R6)n)p]q-B, R9R10NCO, (substituted) heterocyclyl; R3, R4, R5, R6, R9 and R10 = H, C1-6 alkyl, C2-7 alkenyl, C2-7 alkynyl, hydroxy-C1-6 alkyl, etc.; B = C2-7 alkenyl, C2-7 alkynyl, Ho-C1-6 alkyl, C2-12 alkylthioalkyl, etc.; A = CH2, O, S, SO, R7N, R7P, NHCO, NHSO, R7PO eherein R7 = H, C1-6 alkyl, C7-10 aralkyl, alkyl(dialkyl)aminoalkyl, etc.; m, n = 0-6; p, q = 0,1) or a salt thereof, useful as immunosuppressants (data) antiinflammatories, antiproliferating and antitumor agents (no data), are prepared I [R1 = p-(O2N)C6H4CO2, R2 = H] in CH2Cl2 was treated at -10° under N with 2-(2- aminoethyl)pyridine to give after workup I [R1 = 2-(pyridin-2- yl)ethylcarbamoyl, R2 = H] which was converted to the HCl salt (II). In an in vivo test for evaluating immunosuppressive activity, the survival time of pinch skin graft of II at 4 mg/kg was 11.40 days vs. controls which was 6-7 days.

MSTR 1



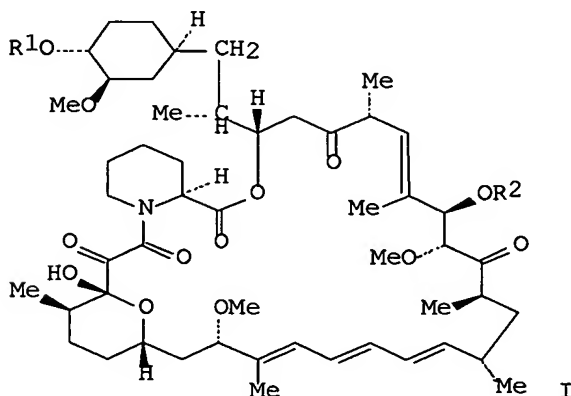
G1 = (-1) OH  
 G4 = 71



DER: and pharmaceutically acceptable salts  
 MPL: claim 1

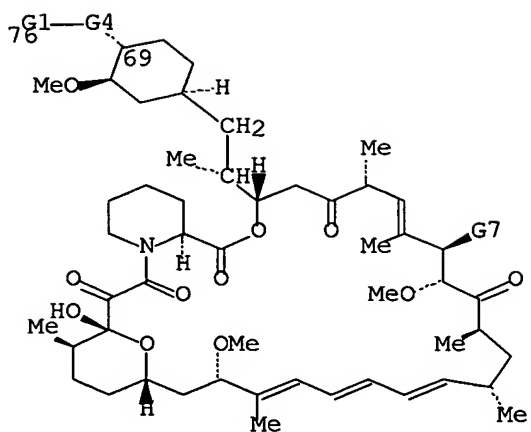
L8 ANSWER 13 OF 15 MARPAT COPYRIGHT 2005 ACS on STN  
 AN 121:73883 MARPAT Full-text  
 TI O-heteroaryl, O-alkylheteroaryl, O-alkenylheteroaryl and  
 O-alkynylheteroarylrapamycin derivatives for treatment of autoimmune,  
 inflammatory, and other diseases  
 IN Parsons, William H.; Sinclair, Peter J.; Wong, Frederick; Wyvratt,  
 Matthew  
 J.  
 PA Merck and Co., Inc., USA  
 SO U.S., 34 pp.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	US 5310901	A	19940510	US 1993-26926	19930305
PRAI	US 1993-26926		19930305		
GI					



AB O-heteroaryl, O-alkylheteroaryl, O-alkenylheteroaryl and O-alkynylheteroarylrapamycin derivs. I (R1 = heteroaryl, substituted heteroaryl, heteroaryl-C1-10 alkyl, etc.; R2 = R1, H, Ph, substituted Ph, 1- or 2-naphthyl, etc.) have been prepared from suitable precursors by alkylation and/or arylation at C-42 and/or C-31. These compds. are useful in a mammalian host for the treatment of autoimmune diseases and diseases of inflammation, infectious diseases, the prevention of rejection of foreign organ transplants, and the treatment of solid tumors. Preparation of selected I is included. 42-(1-Hydroxyethylindol-5-yl)oxyrapamycin inhibited proliferation of T-cells.

MSTR 1



G7 = OH

G10 = PO<sub>3</sub>H<sub>2</sub>

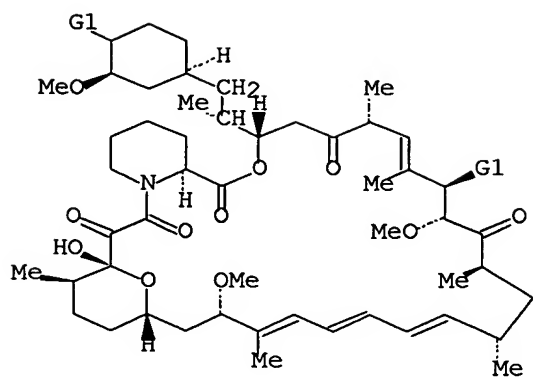
DER: or pharmaceutically acceptable salts

MPL: claim 1

NTE: alkylenes and alkenyls in G5 and ak in G6 may be optionally interrupted







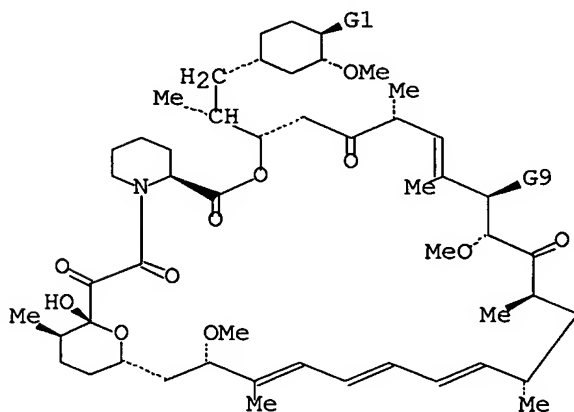
G1 = (-) OH  
 G16 = PO<sub>3</sub>H<sub>2</sub>  
 DER: or pharmaceutically acceptable salts  
 MPL: claim 1

L8 ANSWER 15 OF 15 MARPAT COPYRIGHT 2005 ACS on STN  
 AN 118:80729 MARPAT Full-text  
 TI (carbamoyl)rapamycin derivatives, a method for their preparation and their use as immunosuppressants  
 IN Kao, Wenling; Vogel, Robert Lewis; Musser, John Henry  
 PA American Home Products Corp., USA  
 SO Eur. Pat. Appl., 16 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 509795	A2	19921021	EP 1992-303401	19920415
	EP 509795	A3	19940323		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE				
	US 5118678	A	19920602	US 1991-686728	19910417
	US 5194447	A	19930316	US 1992-837048	19920218
	CA 2065791	AA	19930819	CA 1992-2065791	19920410
	US 5262424	A	19931116	US 1992-977380	19921117
PRAI	US 1991-686728		19910417		
	US 1992-837048		19920218		
OS	CASREACT 118:80729				

AB Some rapamycin carbamate derivs. are claimed. Pharmaceuticals containing said compds. are claimed. A mixture of rapamycin, pyridine, and 4-fluorophenyl isocyanate was stirred at 0° for 5 h to give rapamycin 42-[(4-fluorophenyl)carbamate] (I). The immunosuppressant activity of I was demonstrated in a thymocyte proliferation test, mixed lymphocyte reaction and in the survival of a pinch skin graft on mice.

#### MSTR 1A



G7 = PO3H2  
 G9 = OH  
 DER: or pharmaceutically acceptable salts  
 MPL: claim 1  
 NTE: substitution is restricted

=> d l1; d his; log y  
L1 HAS NO ANSWERS  
L1 STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.

(FILE 'HOME' ENTERED AT 16:55:33 ON 15 FEB 2005)

FILE 'REGISTRY' ENTERED AT 16:55:43 ON 15 FEB 2005

L1 STRUCTURE UPLOADED  
L2 1 S L1  
L3 14 S L1 FUL

FILE 'CAPLUS' ENTERED AT 16:56:18 ON 15 FEB 2005

L4 5 S L3

FILE 'MARPAT' ENTERED AT 16:57:00 ON 15 FEB 2005

L5 0 S L3  
L6 18 S L3 FUL  
L7 18 S L1 FUL  
L8 15 S L7 NOT L4

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-10.20	-13.85

STN INTERNATIONAL LOGOFF AT 16:58:28 ON 15 FEB 2005